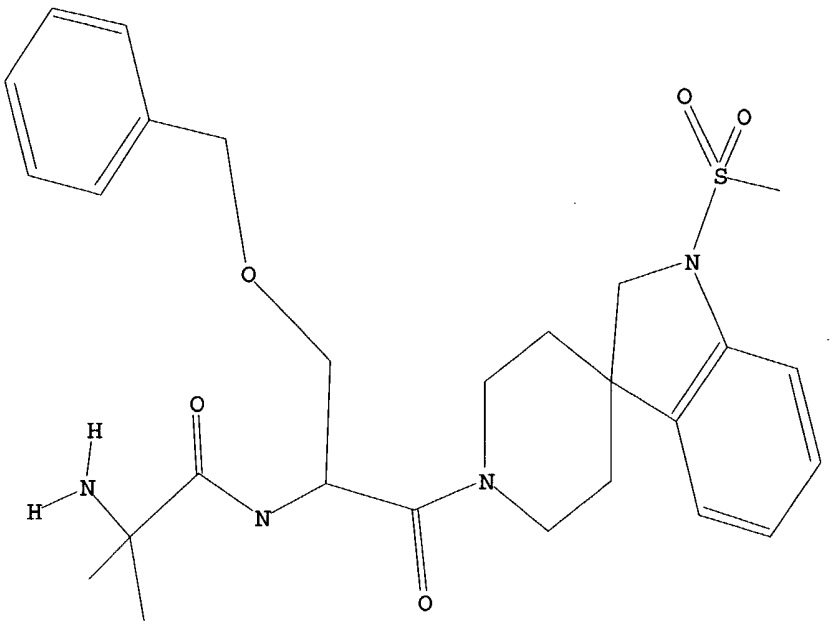
5/13/2004

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **304853-26-7** REGISTRY
CN Ghrelin (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Growth hormone secretagogue



Structure attributes must be viewed using STN Express query preparation.

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=> s l1
SAMPLE SEARCH INITIATED 14:54:50 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     14 TO ITERATE

100.0% PROCESSED      14 ITERATIONS                                4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           56 TO      504
PROJECTED ANSWERS:               4 TO      200

L2            4 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 14:54:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    204 TO ITERATE

100.0% PROCESSED     204 ITERATIONS                              37 ANSWERS
SEARCH TIME: 00.00.01

L3           37 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                             155.42     155.63
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5/13/2004

FILE 'CAPLUS' ENTERED AT 14:54:59 ON 19 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


FILE COVERS 1907 - 19 May 2004 VOL 140 ISS 21
FILE LAST UPDATED: 18 May 2004 (20040518/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l3
L4          105 L3

=> s l3 and (food or diabetes or anorexia or  or lack of appetite)
MISSING TERM 'OR  OR'
The search profile that was entered contains a logical
operator followed immediately by another operator.

=> s l3 and (food or diabetes or anorexia or lack of appetite)
            105 L3
         291349 FOOD
          66103 FOODS
         310265 FOOD
                (FOOD OR FOODS)
          88894 DIABETES
           5286 ANOREXIA
              7 ANOREXIAS
           5286 ANOREXIA
                (ANOREXIA OR ANOREXIAS)
         136367 LACK
          18410 LACKS
         153525 LACK
                (LACK OR LACKS)
          20366 APPETITE
            170 APPETITES
          20450 APPETITE
                (APPETITE OR APPETITES)
             60 LACK OF APPETITE
                (LACK(1W)APPETITE)
L5            6 L3 AND (FOOD OR DIABETES OR ANOREXIA OR LACK OF APPETITE)

=> d abs bib hitstr 1-6
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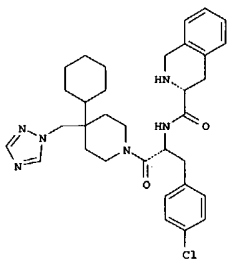
L5 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI

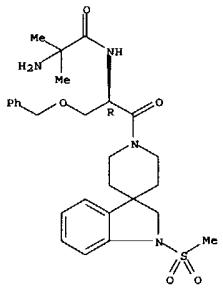


I

AB Synthetic and natural peptides that act as nonselective melanocortin receptor agonists have been found to be anorexigenic and to stimulate erectile activity. We report the design and development of (I), a potent, selective (1184-fold vs. MC3R, 350-fold vs. MC5R), small-mol. agonist of the MC4 receptor. Pharmacol. testing confirms the **food** intake lowering effects of MC4R agonism and suggests another role for the receptor in the stimulation of erectile activity.
AN 2002:699493 CAPLUS
DN 137:362928
TI Design and pharmacology of N-[(3R)-1,2,3,4-tetrahydroisoquinolinium-3-ylcarbonyl]-(1R)-1-(4-chlorobenzyl)-2-[4-cyclohexyl-4-(1H-1,2,4-triazol-1-ylmethyl)piperidin-1-yl]-2-oxoethylamine (1), a potent, selective, melanocortin subtype-4 receptor agonist
AU Sebhat, Iyassu K.; Martin, William J.; Ye, Zhixiong; Barakat, Khaled; Mosley, Ralph T.; Johnston, David B. R.; Bakshi, Raman; Palucki, Brenda; Weinberg, David H.; MacNeil, Tanya; Kalyani, Rubana N.; Tang, Rui; Stearns, Ralph A.; Miller, Randy R.; Tamvakopoulos, Constantin; Strack, Alison M.; McGowan, Erin; Cashen, Doreen E.; Driskо, Jennifer E.; Hom, Gary J.; Howard, Andrew D.; MacIntyre, D. Euan; van der Ploeg, Lex H. T.; Patchett, Arthur A.; Nargund, Ravi P.
CS Departments of Chemistry, Pharmacology, Obesity Research, and Drug Metabolism, Merck Co. Inc., Rahway, NJ, 07065-0900, USA
SO Journal of Medicinal Chemistry (2002), 45(21), 4589-4593
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English

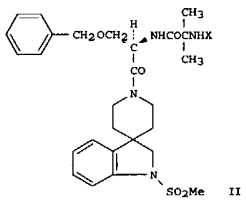
L5 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **159634-47-6**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(design and pharmacol. of melanocortin 4 receptor agonist)
RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



II

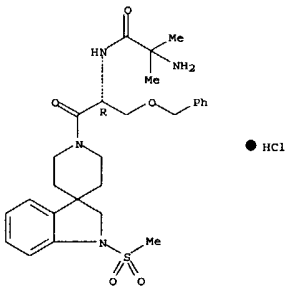
AB This invention is concerned with polymorphic forms of the compound N-[1(R)-[(1,2-dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperdin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonate (I). I is a growth hormone secretagogue that is useful in **food** animals to promote their growth thereby rendering the production of edible meat products more efficient, and in humans, to treat physiol. or medical conditions. The present invention is also concerned with the formulations in the treatment of certain disorders. Thus, compound (II; X = BOC) (preparation given) was treated with MeSO3H to give the title compound II.MeSO3H (X = H).
AN 1998:414732 CAPLUS
DN 129:67698
TI Polymorphic forms of a growth hormone secretagogue
IN Draper, Jerome P.; Kaufman, Michael J.; Dubost, David C.; McCauley, James A.; Vandrilla, Jennifer L.; Varsolona, Richard J.
PA Merck and Co., Inc., USA
SO U.S., 25 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 5767124 | A | 19980616 | US 1996-736170 | 19961023 |
| CN 1205703 | A | 19990120 | CN 1996-199328 | 19961023 |
| CN 1067687 | B | 20010627 | | |
| PRAI US 1996-736170 | A | 19961023 | | |

OS CASREACT 129:67698
IT **159633-92-8P 159634-47-6P 159752-10-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminomethylpropanamide derivs. for the treatment of physiol. or medical conditions and certain disorders)
RN 159633-92-8 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-

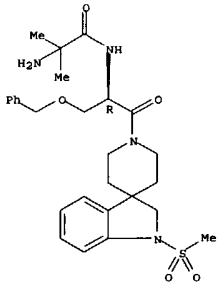
L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



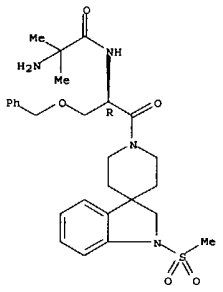
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-

L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.

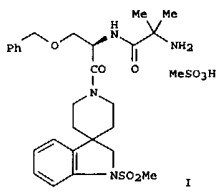


CM 2

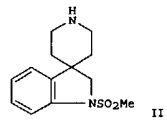
CRN 75-75-2
CMF C H4 O3 S

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I



II

AB A novel convergent process for the preparation of the compound
N-[1(R)-[(1,2-dihydro-1-methanesulfonyl-spiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonamide (I) is claimed. The above compound I is synthesized from the reactants (R)-PhCH2OCH2CH(NH2)CO2Me, BocNHC(Me2)CO2H and spiro compound II (which is synthesized in several steps from isonipecotic acid, PhNHNH2 and MeSO2Cl) with an overall yield of 56% and 99.9% purity. This compound may be used to treat conditions which require the stimulation of growth hormone production, or secretion such as in humans with a deficiency of natural growth hormone, or in animals used for food or wool production where the stimulation of growth hormone will result in a larger, more productive animal.
AN 1998:293521 CAPLUS
DN 128:321949
TI Preparation of N-[1(R)-[(1,2-dihydro-1-methanesulfonyl-spiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonamide, a growth hormone secretagogue
IN Dorziotis, Ilias; Houpis, Ioannis; Molina, Audrey; Volante, Ralph
PA Merck & Co., Inc., USA; Dorziotis, Ilias; Houpis, Ioannis; Molina, Audrey; Volante, Ralph
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9818815 | A1 | 19980507 | WO 1997-US19063 | 19971021 |

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

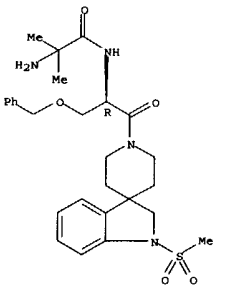
| | | | | |
|---|---|---|---|---|
| AU 9749934 | A1 | 19980522 | AU 1997-49934 | 19971021 |
| US 6046333 | A | 20000404 | US 1997-955124 | 19971021 |
| PRAI US 1996-29454P | P | 19961025 | | |
| GB 1996-25815 | A | 19961212 | | |
| WO 1997-US19063 | W | 19971021 | | |

IT **159752-10-0P**
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of spiroindolepiperidinyl derivative of aminoisobutyrylserinamide as a growth hormone secretagogue)
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.



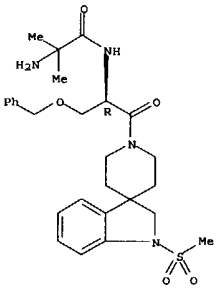
CM 2

CRN 75-75-2
CMF C H4 O3 S

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

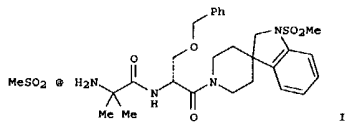
IT **159634-47-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of spiroindolepiperidinyl derivative of aminoisobutyrylserinamide as a growth hormone secretagogue)
RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



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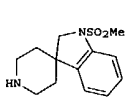

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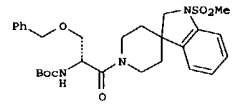


III

AB The present invention is directed to a novel process for the preparation of N-[1(R)-[(1,2-dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperdin]-1'-yl)carbonyl]-2-(benzyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonate (I) and which has the ability to stimulate the release of natural or endogenous growth hormone. I may be used to treat conditions which require the stimulation of growth hormone production or secretion such as in humans with a deficiency of natural growth hormone or in animals used for **food** or wool production where the stimulation of growth hormone will result in a larger, more productive animal. Thus, peptide coupling of spiropiperidine II (preparation given) with Boc-D-Ser(CH2Ph)-OH (Boc = Me3CO2C) in the presence of DCC and HOBt in aqueous iso-Pr acetate gave 93% adduct III, which was deprotected with MeSO3H in MeOH or EtOH, further coupled with Boc-Aib-OH (Aib = α-aminoisobutyric acid) using DCC and HOBt in aqueous iso-Pr acetate, deprotected with MeSO3H in EtOH, and converted into salt I with MeSO3H in EtOAc.

AN 1998:165466 CAPLUS
DN 128:205149
TI Process for the preparation of a growth hormone secretagogue
IN Houghton, Peter G.; Molina, Audrey; Houpis, Joannis; Lynch, Joseph E.; Volante, Ralph P.
PA Merck and Co., Inc., USA
SO U.S., 24 pp.
CODEN: USXXAM

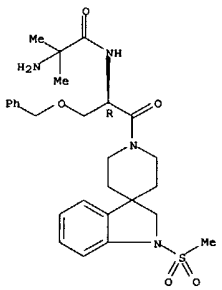
L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 5723616 | A | 19980303 | US 1996-736173 | 19961023 |
| PRAI US 1996-736173 | | 19961023 | | |

OS CASREACT 128:205149
IT **159634-47-6DP**, N-protected deriva. **159634-47-6P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of growth hormone secretagogue using DCC in aqueous iso-Pr acetate)
RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

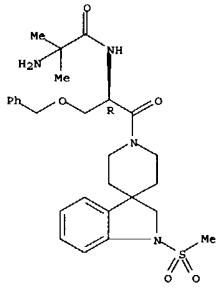
Absolute stereochemistry.



RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



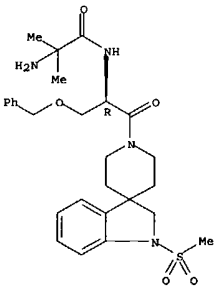
IT **159752-10-0P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of growth hormone secretagogue using DCC in aqueous iso-Pr acetate)
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



CM 2

CRN 75-75-2
CMF C H4 O3 S

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

AB A review with 183 refs. Growth hormone-releasing peptides (GHRPs) are synthetic, non-natural peptides endowed with potent stimulatory effects on somatotrope secretion in animals and humans. They have no structural homol. with GHRH and act via specific receptors present either at the pituitary or the hypothalamic level both in animals and in humans. The GHRP receptor has been cloned and, interestingly, it does not show sequence homol. with other G-protein-coupled receptors known so far. This evidence strongly suggests the existence of a natural GHRP-like ligand which, however, has not yet been found. The mechanisms underlying the GHRP effect are still unclear. At present, several data favor the hypothesis that GHRPs could act by counteracting somatostatinergic activity both at the pituitary and the hypothalamic level and/or, at least partially, via a GHRH-mediated mechanism. However, the possibility that GHRPs act via an unknown hypothalamic factor (U factor) is still open. GHRP-6 was the first hexapeptide to be extensively studied in humans. More recently, a heptapeptide, GHRP-1, and two other hexapeptides, GHRP-2 and Hexarelin, have been synthesized and are now available for human studies. Moreover, non-peptidyl GHRP mimetics have been developed which act via GHRP receptors and their effects have been clearly demonstrated in animals and in humans in vivo. Among non-peptidyl GHRPs, MK-0677 seems the most interesting mol. The GH-releasing activity of GHRPs is marked and dose-related after i.v., s.c., intranasal and even oral administration. The effect of GHRPs is reproducible and undergoes partial desensitization, more during continuous infusion, less during intermittent administration: in fact, prolonged administration of GHRPs increases IGF-I levels both in animals and in humans. The GH-releasing effect of GHRPs does not depend on sex but undergoes age-related variations. It increases from birth to puberty, persists at a similar level in adulthood and decreases thereafter. By the sixth decade of life, the activity of GHRPs is reduced but it is still marked and higher than that of GHRH. The GH-releasing activity of GHRPs is synergistic with that of GHRH, is not affected by opioid receptor antagonists, such as naloxone, and is only blunted by inhibitory influences, including neurotransmitters, glucose, free fatty acids, glucocorticoids, recombinant human GH and even exogenous somatostatin, which are known to almost abolish the effect of GHRH. GHRPs maintain their GH-releasing effect in somatotrope hypersecretory states such as in acromegaly, **anorexia** nervosa and hyperthyroidism. Their good GH-releasing activity has been shown in some but not in other somatotrope hyposecretory states. In fact, reduced GH responses after GHRP administration have been reported in idiopathic GH deficiency as well as in idiopathic short stature, in obesity and in hypothyroidism, while in patients with pituitary stalk disconnection or Cushing's syndrome the somatotrope responsiveness to GHRPs is almost absent. In short children an increase in height velocity has also been reported during chronic GHRP treatment. Thus, based on their marked GH-releasing effect even after oral administration, GHRPs offer their own clin. usefulness for treatment of some GH hyposecretory states.

AN 1997:375774 CAPLUS

DN 127:90522

TI Growth hormone-releasing peptides

AU Ghigo, E.; Arvat, E.; Muccioli, G.; Camanni, F.

CS Division of Endocrinology, Dep. of Internal Medicine and Division of Pharmacology, Dep. of Anatomy, Pharmacology and Forensic Medicine, University of Turin, Italy

SO European Journal of Endocrinology (1997), 136(5), 445-460
CODEN: EJOEEP; ISSN: 0804-4643

PB BioScientifica

DT Journal; General Review

LA English

IT **159752-10-0**, MK 677
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(growth hormone-releasing peptides)

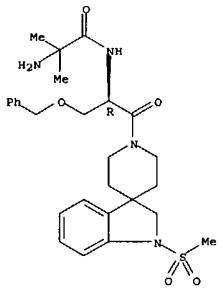
RN 159752-10-0 CAPLUS

CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4''-piperidin]-1''-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.



L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CM 2

CRN 75-75-2
CMF C H4 O3 S

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB There are disclosed certain novel compds. identified as spiro piperidines and homologs I and II wherein: R1 = e.g., C1-10 alkyl, aryl, aryl-(C1-6 alkyl); R2 = e.g., H, C1-6 alkyl, C3-7 cycloalkyl; R3a and R3b are independently, e.g., H, halo, C1-6 alkyl; R4 and R5 are independently, H, C1-6 alkyl, substituted C1-6 alkyl where the substituents on alkyl are, e.g., 1 to 5 halo, 1 to 3 hydroxy; R6 is H or C1-6 alkyl; A is (CH2)xCR7R7a(CH2)y or Z(CH2)xCR7R7a(CH2)y wherein x and y are independently 0, 1, 2, or 3; Z is NR2 or O; R7 and R7a are independently, e.g., H, C1-6 alkyl, OR2; B, D, E, and F are independently selected from CR8R10, O, CO, SOm, NR9, wherein one or two of B, D, E, or F may be optionally absent to provide a 5, 6, or 7-membered ring; R8 and R10 are independently, e.g., H, R2, OR2; R9 = e.g., R2, COR2, SO2R2; m is 0, 1, or 2; n is 1 or 2; G, H, I and J are carbon, nitrogen, sulfur or oxygen atoms, such that one or two is a heteroatom, and where one of G, H, I or J may be optionally absent to afford a 5 or 6 membered heterocyclic aromatic ring; and the pharmaceutically acceptable salts and individual diastereomers thereof, which promote the release of growth hormone in humans and animals (no data). This property can be utilized to promote the growth of **food** animals to render the production of edible meat products more efficient, and in humans, to treat physiol. or medical conditions characterized by a deficiency in growth hormone secretion, such as short stature in growth hormone deficient children, and to treat medical conditions which are improved by the anabolic effects of growth hormone. Growth hormone releasing compns. containing such spiro compds. as the active ingredient thereof are also disclosed. Thus, e.g., 1'-(t-butyloxycarbonyl)spiro[1H-indene-1,4'-piperidine] was subjected to hydroboration/oxidation, to provide 1'-(t-butyloxycarbonyl)-2,3-dihydro-3-oxospiro[1H-indene-1,4'-piperidine]; deprotection followed by trifluoroacetylation afforded the trifluoroacetamide; Schmidt reaction of the latter provided 3,4-dihydro-2-oxospiro[piperidine-4,4'(1H)-quinoline] trifluoroacetamide (together with its spiroisoquinoline isomer); saponification followed by coupling with α(R)-[[2-[[(1,1-dimethylethoxy)carbonyl]amino]-2,2-dimethyl-1-oxoethyl]amino]-1H-indole-3-propanoic acid (preparation given) and deprotection provided N-[1(R)-[(3,4-dihydro-2-oxospiro[piperidine-4,4'(1H)-quinolin]-1'-yl)carbonyl]-2-(indol-3-yl)ethyl]-2-amino-2-methylpropanamide hydrochloride (III.HCl).

AN 1996:469925 CAPLUS

DN 125:196372

TI Spiro piperidines which promote release of growth hormone

IN Chen, Meng-Hsin; Johnston, David B. R.; Nargund, Ravi P.; Patchett, Arthur A.; Tata, James R.; Yang, Lihu

PA Merck and Co., Inc., USA

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
SO U.S., 48 pp., Cont.-in-part of U.S. Ser. No. 989,322, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

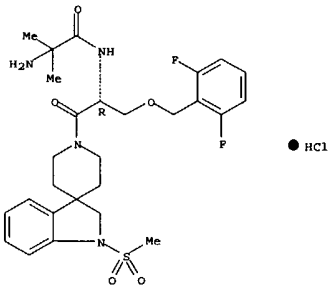
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 5536716 | A | 19960716 | US 1993-147226 | 19931103 |
| WO 9413696 | A1 | 19940623 | WO 1993-US11038 | 19931115 |
| W: BB, BG, BR, BY, CZ, FI, HU, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ | | | | |
| RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| WO 9419367 | A1 | 19940901 | WO 1993-US11137 | 19931115 |
| W: BB, BG, BR, BY, CZ, FI, HU, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ | | | | |
| RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| HU 72076 | A2 | 19960328 | HU 1995-1683 | 19931115 |
| HU 73228 | A2 | 19960729 | HU 1995-1681 | 19931115 |
| PL 176993 | B1 | 19990831 | PL 1993-309331 | 19931115 |
| RU 2168512 | C2 | 20010610 | RU 1995-113349 | 19931115 |
| SK 282166 | B6 | 20011106 | SK 1995-759 | 19931115 |
| CA 2110670 | AA | 19940612 | CA 1993-2110670 | 19931203 |
| CA 2110670 | C | 20010417 | | |
| CA 2110672 | AA | 19940612 | CA 1993-2110672 | 19931203 |
| EP 615977 | A1 | 19940921 | EP 1993-309867 | 19931208 |
| EP 615977 | B1 | 20020703 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| AT 220071 | E | 20020715 | AT 1993-309867 | 19931208 |
| PT 615977 | T | 20021031 | PT 1993-309867 | 19931208 |
| ES 2177538 | T3 | 20021216 | ES 1993-309867 | 19931208 |
| AU 9352320 | A1 | 19940623 | AU 1993-52320 | 19931210 |
| AU 672552 | B2 | 19961114 | | |
| AU 9352321 | A1 | 19940623 | AU 1993-52321 | 19931210 |
| AU 673017 | B2 | 19961024 | | |
| ZA 9309272 | A | 19940808 | ZA 1993-9272 | 19931210 |
| ZA 9309274 | A | 19940808 | ZA 1993-9274 | 19931210 |
| JP 06263737 | A2 | 19940920 | JP 1993-341522 | 19931210 |
| JP 2509530 | B2 | 19960619 | | |
| HR 931486 | B1 | 20030831 | HR 1993-931486 | 19931210 |
| CN 1092071 | A | 19940914 | CN 1993-112858 | 19931211 |
| CN 1034733 | B | 19970430 | | |
| FI 9502862 | A | 19950609 | FI 1995-2862 | 19950609 |
| FI 9502863 | A | 19950609 | FI 1995-2863 | 19950609 |
| NO 9502294 | A | 19950810 | NO 1995-2294 | 19950609 |
| NO 9502295 | A | 19950810 | NO 1995-2295 | 19950609 |
| US 5652235 | A | 19970729 | US 1996-641311 | 19960430 |
| PRAI US 1992-989322 | B2 | 19921211 | | |
| US 1993-146848 | | 19931103 | | |
| US 1993-147226 | A | 19931103 | | |
| WO 1993-US11038 | W | 19931115 | | |
| WO 1993-US11137 | W | 19931115 | | |

OS MARPAT 125:196372
IT **159633-90-6P 159633-92-8P 159633-94-0P**
**159634-09-0P 159634-10-3P 159634-12-5P**
**159634-13-6P 159634-37-4P 159634-47-6P**

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
**159634-49-8P 159634-50-1P 159752-10-0P**
**180465-75-2P 180465-79-6P 180465-80-9P**
**180466-14-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); FFD (Food or feed use); SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(spiro piperidines which promote release of growth hormone)

RN 159633-90-6 CAPLUS
CN Propanamide, 2-amino-N-[1-[[(2,6-difluorophenyl)methoxy]methyl]-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxoethyl]-2-methyl-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

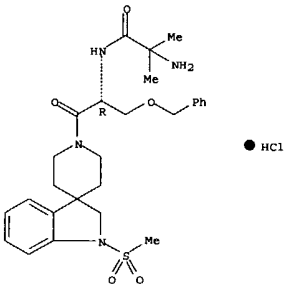
Absolute stereochemistry.



RN 159633-92-8 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

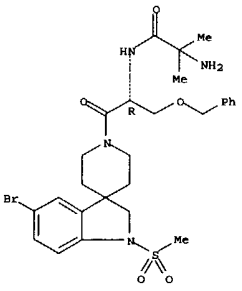


RN 159633-94-0 CAPLUS
CN Propanamide, 2-amino-N-[2-[5-bromo-1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, (R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 159633-93-9
CMF C27 H35 Br N4 O5 S

Absolute stereochemistry.

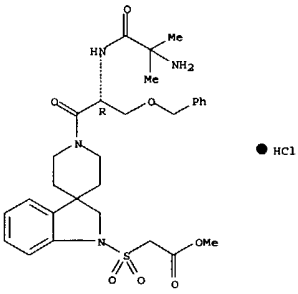


L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 159634-09-0 CAPLUS
CN Acetic acid, [[1'-[2-[(2-amino-2-methyl-1-oxopropyl)amino]-1-oxo-3-(phenylmethoxy)propyl]spiro[3H-indole-3,4'-piperidin]-1(2H)-yl]sulfonyl]-, methyl ester, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

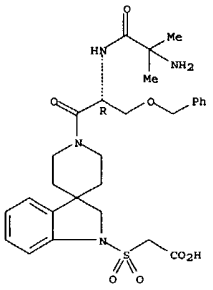
Absolute stereochemistry.



RN 159634-10-3 CAPLUS
CN Acetic acid, [[1'-[2-[(2-amino-2-methyl-1-oxopropyl)amino]-1-oxo-3-(phenylmethoxy)propyl]spiro[3H-indole-3,4'-piperidin]-1(2H)-yl]sulfonyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



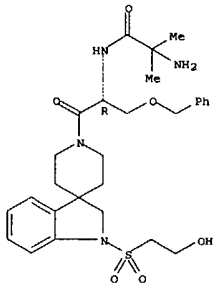
RN 159634-12-5 CAPLUS
CN Propanamide, 2-amino-N-[2-[1,2-dihydro-1-[(2-hydroxyethyl)sulfonyl]spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, (R)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 159634-11-4
CMF C28 H38 N4 O6 S

Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



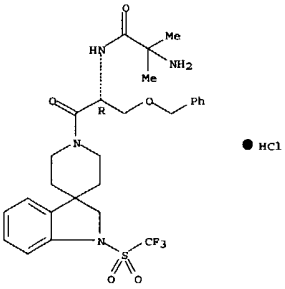
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 159634-13-6 CAPLUS
CN Propanamide, 2-amino-N-[2-[1,2-dihydro-1-[(trifluoromethyl)sulfonyl]spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

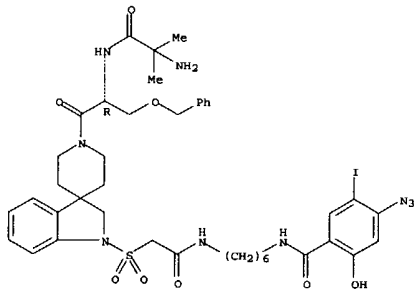


● HCl

RN 159634-37-4 CAPLUS
CN Benzamide, N-[6-[[[[1'-[2-[(2-amino-2-methyl-1-oxopropyl)amino]-1-oxo-3-(phenylmethoxy)propyl]spiro[3H-indole-3,4'-piperidin]-1(2H)-yl]sulfonyl]acetyl]amino]hexyl]-4-azido-2-hydroxy-5-iodo-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



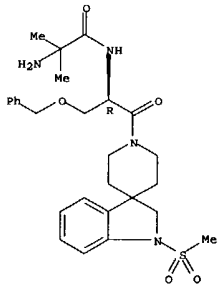
L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A

● HCl

RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

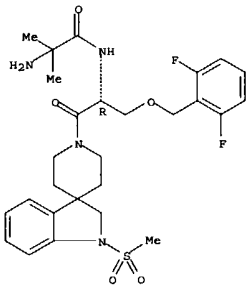
Absolute stereochemistry.



RN 159634-49-8 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-1-[[(2,6-difluorophenyl)methoxy]methyl]-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxoethyl]-2-methyl- (9CI) (CA INDEX NAME)

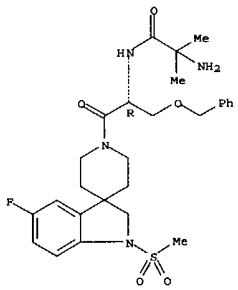
Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



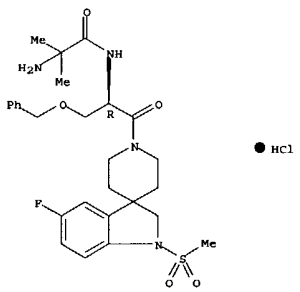
RN 159634-50-1 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[5-fluoro-1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



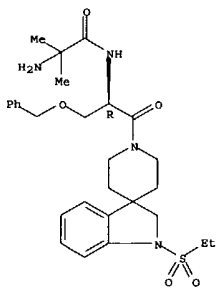
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 180465-79-6 CAPLUS
CN Propanamide, 2-amino-N-[2-[1-(ethylsulfonyl)-1,2-dihydrospiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 180465-80-9 CAPLUS
CN Propanamide, 2-amino-N-[2-[1,2-dihydro-1-[(1-methylethyl)sulfonyl]spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

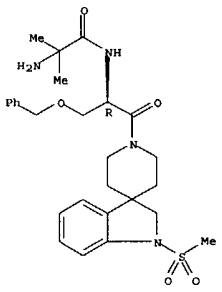


L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.



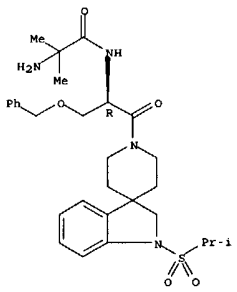
CM 2

CRN 75-75-2
CMF C H4 O3 S

RN 180465-75-2 CAPLUS
CN Propanamide, 2-amino-N-[2-[5-fluoro-1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RN 180466-14-2 CAPLUS
CN Acetic acid, [[1'-[N-(2-methylalanyl)-O-(phenylmethyl)-D-seryl]spiro[3H-indole-3,4'-piperidin]-1(2H)-yl]sulfonyl]-, 6-[[5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-1-oxopentyl]amino]hexyl ester, [3aS-(3aα,4β,6aα)]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

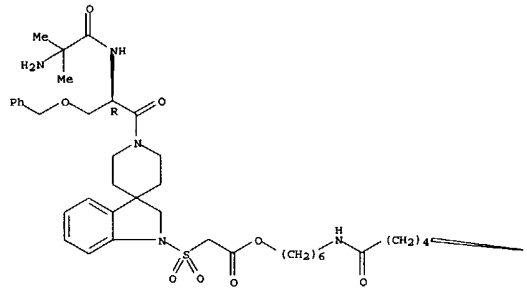
CM 1

CRN 180466-13-1
CMF C44 H63 N7 O9 S2

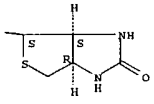
Absolute stereochemistry.

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

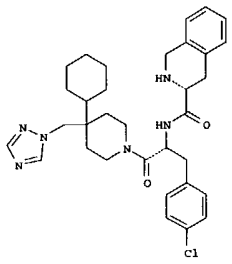
CM 2

CRN 76-05-1
CMF C2 H F3 O2

5/13/2004

=> d abs bib fhitstr 1-6

L5 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI

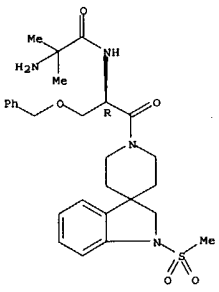


I

AB Synthetic and natural peptides that act as nonselective melanocortin receptor agonists have been found to be anorexigenic and to stimulate erectile activity. We report the design and development of (I), a potent, selective (1184-fold vs. MC3R, 350-fold vs. MC5R), small-mol. agonist of the MC4 receptor. Pharmacol. testing confirms the **food** intake lowering effects of MC4R agonism and suggests another role for the receptor in the stimulation of erectile activity.
AN 2002:699493 CAPLUS
DN 137:362928
TI Design and pharmacology of N-[(3R)-1,2,3,4-tetrahydroisoquinolinium-3-ylcarbonyl]-(1R)-1-(4-chlorobenzyl)-2-[4-cyclohexyl-4-(1H-1,2,4-triazol-1-ylmethyl)piperidin-1-yl]-2-oxoethylamine (1), a potent, selective, melanocortin subtype-4 receptor agonist
AU Sebhat, Iyassu K.; Martin, William J.; Ye, Zhixiong; Barakat, Khaled; Mosley, Ralph T.; Johnston, David B. R.; Bakshi, Raman; Palucki, Brenda; Weinberg, David H.; MacNeil, Tanya; Kalyani, Rubana N.; Tang, Rui; Stearns, Ralph A.; Miller, Randy R.; Tamvakopoulos, Constantin; Strack, Alison M.; McGowan, Erin; Cashen, Doreen E.; Drisko, Jennifer E.; Hom, Gary J.; Howard, Andrew D.; MacIntyre, D. Euan; van der Ploeg, Lex H. T.; Patchett, Arthur A.; Nargund, Ravi P.
CS Departments of Chemistry, Pharmacology, Obesity Research, and Drug Metabolism, Merck Co. Inc., Rahway, NJ, 07065-0900, USA
SO Journal of Medicinal Chemistry (2002), 45(21), 4589-4593
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English

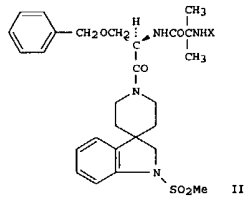
L5 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **159634-47-6**
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(design and pharmacol. of melanocortin 4 receptor agonist)
RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



II

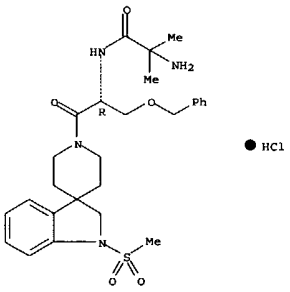
AB This invention is concerned with polymorphic forms of the compound N-[1(R)-[(1,2-dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperdin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonate (I). I is a growth hormone secretagogue that is useful in **food** animals to promote their growth thereby rendering the production of edible meat products more efficient, and in humans, to treat physiol. or medical conditions. The present invention is also concerned with the formulations in the treatment of certain disorders. Thus, compound (II; X = BOC) (preparation given) was treated with MeSO3H to give the title compound II.MeSO3H (X = H).
AN 1998:414732 CAPLUS
DN 129:67698
TI Polymorphic forms of a growth hormone secretagogue
IN Draper, Jerome P.; Kaufman, Michael J.; Dubost, David C.; McCauley, James A.; Vandrilla, Jennifer L.; Varsolona, Richard J.
PA Merck and Co., Inc., USA
SO U.S., 25 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 5767124 | A | 19980616 | US 1996-736170 | 19961023 |
| CN 1205703 | A | 19990120 | CN 1996-199328 | 19961023 |
| CN 1067687 | B | 20010627 | | |
| PRAI US 1996-736170 | A | 19961023 | | |

OS CASREACT 129:67698
IT **159633-92-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminomethylpropanamide derivs. for the treatment of physiol. or medical conditions and certain disorders)
RN 159633-92-8 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-

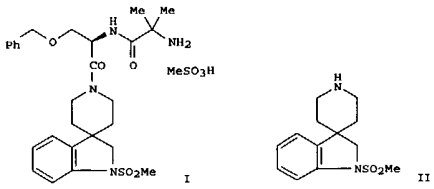
L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I



II

AB A novel convergent process for the preparation of the compound N-[1(R)-[(1,2-dihydro-1-methanesulfonyl-spiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonamide (I) is claimed. The above compound I is synthesized from the reactants (R)-PhCH2OCH2CH(NH2)CO2Me, BocNHC(Me2)CO2H and spiro compound II (which is synthesized in several steps from isonipecotic acid, PhNHNH2 and MeSO2Cl) with an overall yield of 56% and 99.9% purity. This compound may be used to treat conditions which require the stimulation of growth hormone production, or secretion such as in humans with a deficiency of natural growth hormone, or in animals used for **food** or wool production where the stimulation of growth hormone will result in a larger, more productive animal.

AN 1998:293521 CAPLUS
DN 128:321949
TI Preparation of N-[1(R)-[(1,2-dihydro-1-methanesulfonyl-spiro[3H-indole-3,4'-piperidin]-1'-yl)carbonyl]-2-(phenylmethyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonamide, a growth hormone secretagogue
IN Dorziotis, Ilias; Houpis, Ioannis; Molina, Audrey; Volante, Ralph
PA Merck & Co., Inc., USA; Dorziotis, Ilias; Houpis, Ioannis; Molina, Audrey; Volante, Ralph
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

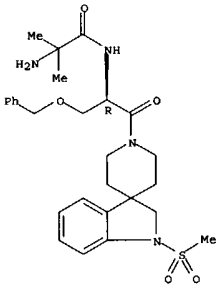
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9818815 | A1 | 19980507 | WO 1997-US19063 | 19971021 |
| W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9749934 | A1 | 19980522 | AU 1997-49934 | 19971021 |
| US 6046333 | A | 20000404 | US 1997-955124 | 19971021 |
| PRAI US 1996-29454P | P | 19961025 | | |
| GB 1996-25815 | A | 19961212 | | |
| WO 1997-US19063 | W | 19971021 | | |

IT **159752-10-0P**
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of spiroindolepiperidinyl derivative of aminoisobutyrylserinamide as a growth hormone secretagogue)
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.



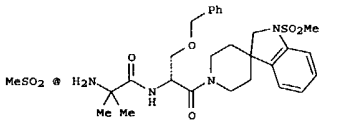
CM 2

CRN 75-75-2
CMF C H4 O3 S

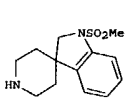
L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

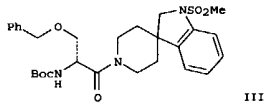
L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I



II



III

AB The present invention is directed to a novel process for the preparation of N-[1(R)-[(1,2-dihydro-1-methanesulfonylspiro[3H-indole-3,4'-piperdin]-1'-yl)carbonyl]-2-(benzyloxy)ethyl]-2-amino-2-methylpropanamide methanesulfonate (I) and which has the ability to stimulate the release of natural or endogenous growth hormone. I may be used to treat conditions which require the stimulation of growth hormone production or secretion such as in humans with a deficiency of natural growth hormone or in animals used for **food** or wool production where the stimulation of growth hormone will result in a larger, more productive animal. Thus, peptide coupling of spiropiperidine II (preparation given) with Boc-D-Ser(CH2Ph)-OH (Boc = Me3CO2C) in the presence of DCC and HOBt in aqueous iso-Pr acetate gave 93% adduct III, which was deprotected with MeSO3H in MeOH or EtOH, further coupled with Boc-Aib-OH (Aib = α-aminoisobutyric acid) using DCC and HOBt in aqueous iso-Pr acetate, deprotected with MeSO3H in EtOH, and converted into salt I with MeSO3H in EtOAc.

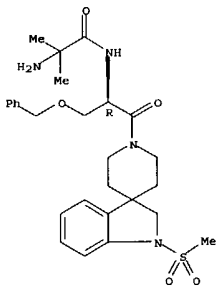
AN 1998:165466 CAPLUS
DN 128:205149
TI Process for the preparation of a growth hormone secretagogue
IN Houghton, Peter G.; Molina, Audrey; Houpis, Joannis; Lynch, Joseph E.; Volante, Ralph P.
PA Merck and Co., Inc., USA
SO U.S., 24 pp.
CODEN: USXXAM
DT Patent
LA English

L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5723616 | A | 19980303 | US 1996-736173 | 19961023 |

PRAI US 1996-736173 19961023
OS CASREACT 128:205149
IT **159634-47-6DP**, N-protected derivs.
RL: IMP (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of growth hormone secretagogue using DCC in aqueous iso-Pr acetate)
RN 159634-47-6 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



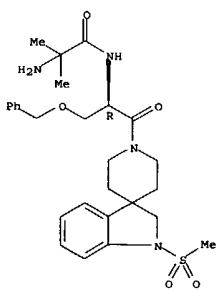
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
AB A review with 183 refs. Growth hormone-releasing peptides (GHRPs) are synthetic, non-natural peptides endowed with potent stimulatory effects on somatotrope secretion in animals and humans. They have no structural homol. with GHRH and act via specific receptors present either at the pituitary or the hypothalamic level both in animals and in humans. The GHRP receptor has been cloned and, interestingly, it does not show sequence homol. with other G-protein-coupled receptors known so far. This evidence strongly suggests the existence of a natural GHRP-like ligand which, however, has not yet been found. The mechanisms underlying the GHRP effect are still unclear. At present, several data favor the hypothesis that GHRPs could act by counteracting somatostatinergic activity both at the pituitary and the hypothalamic level and/or, at least partially, via a GHRH-mediated mechanism. However, the possibility that GHRPs act via an unknown hypothalamic factor (U factor) is still open. GHRP-6 was the first hexapeptide to be extensively studied in humans. More recently, a heptapeptide, GHRP-1, and two other hexapeptides, GHRP-2 and Hexarelin, have been synthesized and are now available for human studies. Moreover, non-peptidyl GHRP mimetics have been developed which act via GHRP receptors and their effects have been clearly demonstrated in animals and in humans in vivo. Among non-peptidyl GHRPs. MK-0677 seems the most interesting mol. The GH-releasing activity of GHRPs is marked and dose-related after i.v., s.c., intranasal and even oral administration. The effect of GHRPs is reproducible and undergoes partial desensitization, more during continuous infusion, less during intermittent administration: in fact, prolonged administration of GHRPs increases IGF-I levels both in animals and in humans. The GH-releasing effect of GHRPs does not depend on sex but undergoes age-related variations. It increases from birth to puberty, persists at a similar level in adulthood and decreases thereafter. By the sixth decade of life, the activity of GHRPs is reduced but it is still marked and higher than that of GHRH. The GH-releasing activity of GHRPs is synergistic with that of GHRH, is not affected by opioid receptor antagonists, such as naloxone, and is only blunted by inhibitory influences, including neurotransmitters, glucose, free fatty acids, glucocorticoids, recombinant human GH and even exogenous somatostatin, which are known to almost abolish the effect of GHRH. GHRPs maintain their GH-releasing effect in somatotrope hypersecretory states such as in acromegaly, **anorexia** nervosa and hyperthyroidism. Their good GH-releasing activity has been shown in some but not in other somatotrope hyposecretory states. In fact, reduced GH responses after GHRP administration have been reported in idiopathic GH deficiency as well as in idiopathic short stature, in obesity and in hypothyroidism, while in patients with pituitary stalk disconnection or Cushing's syndrome the somatotrope responsiveness to GHRPs is almost absent. In short children an increase in height velocity has also been reported during chronic GHRP treatment. Thus, based on their marked GH-releasing effect even after oral administration, GHRPs offer their own clin. usefulness for treatment of some GH hyposecretory states.
AN 1997:375774 CAPLUS
DN 127:90522
TI Growth hormone-releasing peptides
AU Ghigo, E.; Arvat, E.; Muccioli, G.; Camanni, F.
CS Division of Endocrinology, Dep. of Internal Medicine and Division of Pharmacology, Dep. of Anatomy, Pharmacology and Forensic Medicine, University of Turin, Italy
SO European Journal of Endocrinology (1997), 136(5), 445-460
CODEN: EJOEEP; ISSN: 0804-4643
PB BioScientifica
DT Journal; General Review
LA English
IT **159752-10-0**, MK 677
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(growth hormone-releasing peptides)
RN 159752-10-0 CAPLUS
CN Propanamide, 2-amino-N-[(1R)-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxo-1-[(phenylmethoxy)methyl]ethyl]-2-methyl-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 159634-47-6
CMF C27 H36 N4 O5 S

Absolute stereochemistry.



CM 2

CRN 75-75-2

L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CMF C H4 O3 S

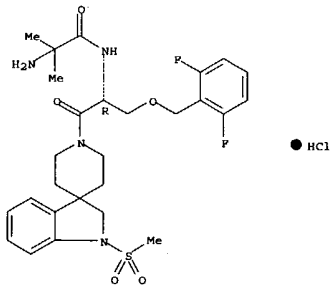
L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB There are disclosed certain novel compds. identified as spiro piperidines and homologs I and II wherein: R1 = e.g., C1-10 alkyl, aryl, aryl-(C1-6 alkyl); R2 = e.g., H, C1-6 alkyl, C3-7 cycloalkyl; R3a and R3b are independently, e.g., H, halo, C1-6 alkyl; R4 and R5 are independently, H, C1-6 alkyl, substituted C1-6 alkyl where the substituents on alkyl are, e.g., 1 to 5 halo, 1 to 3 hydroxy; R6 is H or C1-6 alkyl; A is (CH2)xCR7R7a(CH2)y or Z(CH2)xCR7R7a(CH2)y wherein x and y are independently 0, 1, 2, or 3; Z is NR2 or O; R7 and R7a are independently, e.g., H, C1-6 alkyl, OR2; B, D, E, and F are independently selected from CR8R10, O, CO, SOm, NR9, wherein one or two of B, D, E, or F may be optionally absent to provide a 5, 6, or 7-membered ring; R8 and R10 are independently, e.g., H, R2, OR2; R9 = e.g., R2, COR2, SO2R2; m is 0, 1, or 2; n is 1 or 2; G, H, I and J are carbon, nitrogen, sulfur or oxygen atoms, such that one or two is a heteroatom, and where one of G, H, I or J may be optionally absent to afford a 5 or 6 membered heterocyclic aromatic ring; and the pharmaceutically acceptable salts and individual diastereomers thereof, which promote the release of growth hormone in humans and animals (no data). This property can be utilized to promote the growth of **food** animals to render the production of edible meat products more efficient, and in humans, to treat physiol. or medical conditions characterized by a deficiency in growth hormone secretion, such as short stature in growth hormone deficient children, and to treat medical conditions which are improved by the anabolic effects of growth hormone. Growth hormone releasing compns. containing such spiro compds. as the active ingredient thereof are also disclosed. Thus, e.g., 1'-(t-butyloxycarbonyl)spiro[1H-indene-1,4'-piperidine] was subjected to hydroboration/oxidation, to provide 1'-(t-butyloxycarbonyl)-2,3-dihydro-3-oxospiro[1H-indene-1,4'-piperidine]; deprotection followed by trifluoroacetylation afforded the trifluoroacetamide; Schmidt reaction of the latter provided 3,4-dihydro-2-oxospiro[piperidine-4,4'(1H)-quinoline] trifluoroacetamide (together with its spiroisoquinoline isomer); saponification followed by coupling with α(R)-[[2-[[(1,1-dimethylethoxy)carbonyl]amino]-2,2-dimethyl-1-oxoethyl]amino]-1H-indole-3-propanoic acid (preparation given) and deprotection provided N-[1(R)-[(3,4-dihydro-2-oxospiro[piperidine-4,4'(1H)-quinolin]-1'-yl)carbonyl]-2-(indol-3-yl)ethyl]-2-amino-2-methylpropanamide hydrochloride (III.HCl).
AN 1996:469925 CAPLUS
DN 125:196372
TI Spiro piperidines which promote release of growth hormone

L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
OS MARPAT 125:196372
IT **159633-90-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PFD (Food or feed use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(spiro piperidines which promote release of growth hormone)
RN 159633-90-6 CAPLUS
CN Propanamide, 2-amino-N-[1-[[(2,6-difluorophenyl)methoxy]methyl]-2-[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]-2-oxoethyl]-2-methyl-, monohydrochloride, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IN Chen, Meng-Hsin; Johnston, David B. R.; Nargund, Ravi P.; Patchett, Arthur A.; Tata, James R.; Yang, Lihu
PA Merck and Co., Inc., USA
SO U.S., 48 pp., Cont.-in-part of U.S. Ser. No. 989,322, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5536716 | A | 19960716 | US 1993-147226 | 19931103 |
| | WO 9413696 | A1 | 19940623 | WO 1993-US11038 | 19931115 |
| | W: BB, BG, BR, BY, CZ, FI, HU, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ | | | | |
| | RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | WO 9419367 | A1 | 19940901 | WO 1993-US11137 | 19931115 |
| | W: BB, BG, BR, BY, CZ, FI, HU, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ | | | | |
| | RW: BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | HU 72076 | A2 | 19960328 | HU 1995-1683 | 19931115 |
| | HU 73228 | A2 | 19960729 | HU 1995-1681 | 19931115 |
| | PL 176993 | B1 | 19990831 | PL 1993-309331 | 19931115 |
| | RU 2168512 | C2 | 20010610 | RU 1995-113349 | 19931115 |
| | SK 282166 | B6 | 20011106 | SK 1995-759 | 19931115 |
| | CA 2110670 | AA | 19940612 | CA 1993-2110670 | 19931203 |
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| | EP 615977 | A1 | 19940921 | EP 1993-309867 | 19931208 |
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| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| | AT 220071 | E | 20020715 | AT 1993-309867 | 19931208 |
| | PT 615977 | T | 20021031 | PT 1993-309867 | 19931208 |
| | ES 2177538 | T3 | 20021216 | ES 1993-309867 | 19931208 |
| | AU 9352320 | A1 | 19940623 | AU 1993-52320 | 19931210 |
| | AU 673552 | B2 | 19961114 | | |
| | AU 9352321 | A1 | 19940623 | AU 1993-52321 | 19931210 |
| | AU 673017 | B2 | 19961024 | | |
| | ZA 9309272 | A | 19940808 | ZA 1993-9272 | 19931210 |
| | ZA 9309274 | A | 19940808 | ZA 1993-9274 | 19931210 |
| | JP 06263737 | A2 | 19940920 | JP 1993-341522 | 19931210 |
| | JP 2509530 | B2 | 19960619 | | |
| | HR 931486 | B1 | 20030831 | HR 1993-931486 | 19931210 |
| | CN 1092071 | A | 19940914 | CN 1993-112858 | 19931211 |
| | CN 1034733 | B | 19970430 | | |
| | FI 9502862 | A | 19950609 | FI 1995-2862 | 19950609 |
| | FI 9502863 | A | 19950609 | FI 1995-2863 | 19950609 |
| | NO 9502294 | A | 19950810 | NO 1995-2294 | 19950609 |
| | NO 9502295 | A | 19950810 | NO 1995-2295 | 19950609 |
| | US 5652235 | A | 19970729 | US 1996-641311 | 19960430 |
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| | US 1993-146848 | | 19931103 | | |
| | US 1993-147226 | A | 19931103 | | |
| | WO 1993-US11038 | W | 19931115 | | |
| | WO 1993-US11137 | W | 19931115 | | |

5/13/2004

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 NEWS 18  May 12  EXTEND option available in structure searching
 NEWS 19  May 12  Polymer links for the POLYLINK command completed in REGISTRY
 NEWS 20  May 17  FRFULL now available on STN

 NEWS EXPRESS  MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

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=> file registry
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     2.10       2.10

FILE 'REGISTRY' ENTERED AT 15:50:12 ON 19 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   18 MAY 2004  HIGHEST RN 683203-75-0
DICTIONARY FILE UPDATES:  18 MAY 2004  HIGHEST RN 683203-75-0

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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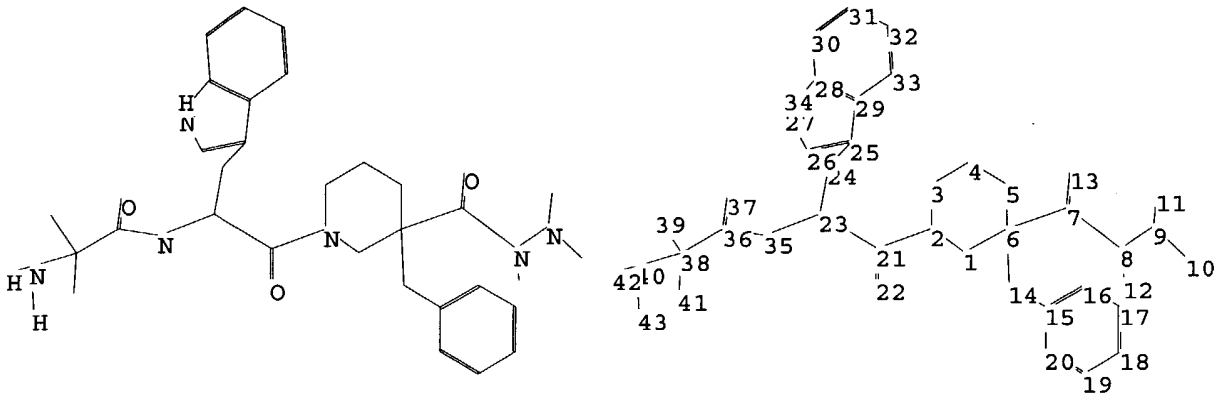
5/13/2004



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7 8 9 10 11 12 13 14 21 22 23 24 34 35 36 37 38 39 40 41 42 43

ring nodes :
1 2 3 4 5 6 15 16 17 18 19 20 25 26 27 28 29 30 31 32 33
chain bonds :
2-21 6-7 6-14 7-8 7-13 8-9 8-12 9-10 9-11 14-15 21-22 21-23 23-24
23-35 24-25 27-34 35-36 36-37 36-38 38-39 38-40 38-41 40-42 40-43
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20 25-26
25-29 26-27 27-28 28-29 28-30 29-33 30-31 31-32 32-33
exact/norm bonds :
1-2 1-6 2-3 2-21 3-4 4-5 5-6 7-8 7-13 8-9 8-12 9-10 9-11 21-22 23-35
25-26 25-29 26-27 27-28 35-36 36-37 38-40
exact bonds :
6-7 6-14 14-15 21-23 23-24 24-25 27-34 36-38 38-39 38-41 40-42 40-43
normalized bonds :
15-16 15-20 16-17 17-18 18-19 19-20 28-29 28-30 29-33 30-31 31-32 32-33

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
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28:Atom 29:Atom 30:Atom 31:Atom 32:Atom 33:Atom 34:CLASS 35:CLASS 36:CLASS
37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 43:CLASS

L1 STRUCTURE UPLOADED

=> d l1

5/13/2004

L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 1 ANSWERS
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FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2 TO 124
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 ful
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FULL SCREEN SEARCH COMPLETED - 33 TO ITERATE

100.0% PROCESSED 33 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

L3 5 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 155.42 157.52

FILE 'CAPLUS' ENTERED AT 15:50:42 ON 19 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


FILE COVERS 1907 - 19 May 2004 VOL 140 ISS 21
FILE LAST UPDATED: 18 May 2004 (20040518/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

5/13/2004

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L4            3 L3

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         291349 FOOD
          66103 FOODS
         310265 FOOD
                   (FOOD OR FOODS)
           5286 ANOREXIA
              7 ANOREXIAS
           5286 ANOREXIA
                   (ANOREXIA OR ANOREXIAS)
          88894 DIABETES
          99841 WEIGHT
          12585 WEIGHTS
         108143 WEIGHT
                   (WEIGHT OR WEIGHTS)
        1355317 WT
         100236 WTS
        1406446 WT
                   (WT OR WTS)
        1436145 WEIGHT
                   (WEIGHT OR WT)
L5            1 L4 AND (FOOD OR ANOREXIA OR DIABETES OR WEIGHT)

=> d abs bib hitstr
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L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

AB Compds. that are liganda for the receptor GHS-R 1A, as well as pharmaceutically acceptable salts thereof, are useful for the manufacture of medicaments for the regulation of **food** intake.

AN 2001:581723 CAPLUS
DN 135:147451

TI Use of compounds for the regulation of **food** intake

IN Andersen, Maibritt Bansholm; Hansen, Birgit Sehested; Raun, Kirsten; Tullin, Soren; Thim, Lars
PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
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| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2001020012 | A1 | 20010906 | US 2001-771770 | 20010129 |
| | US 2004063636 | A1 | 20040401 | US 2003-649386 | 20030827 |
| PRAI | DK 2000-161 | A | 20000201 | | |
| | DK 2000-1107 | A | 20000717 | | |
| | US 2000-181303P | P | 20000209 | | |
| | US 2001-771770 | B1 | 20010129 | | |

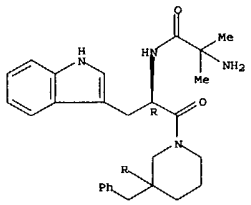
IT **353289-95-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(use of compds. for regulation of **food** intake that are liganda of growth hormone secretagogue type 1A receptors (GHS-R 1A) in relation to growth hormone release)

RN 353289-95-9 CAPLUS
CN 3-Piperidinecarboxylic acid, 1-(2-methylalanyl-D-tryptophyl)-3-(phenylmethyl)-, trimethylhydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Currently available stereo shown.

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

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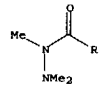


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

5/13/2004

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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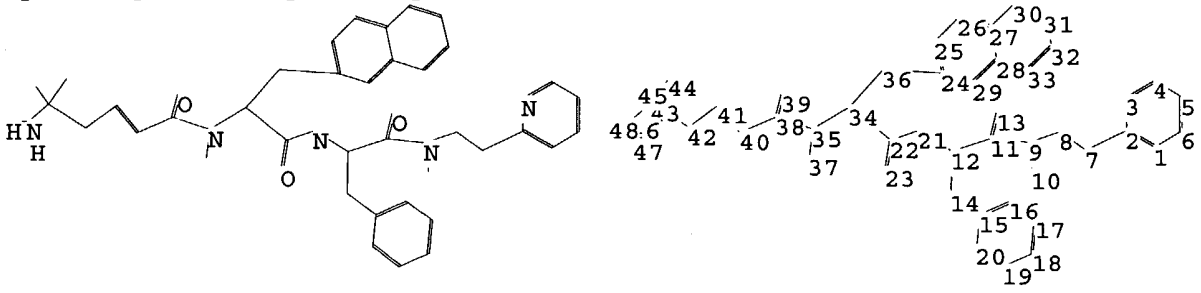

chain nodes :
7 8 9 10 11 12 13 14 21 22 23 34 35 36 37 38 39 40 41 42 43 44
45 46 47 48
ring nodes :
1 2 3 4 5 6 15 16 17 18 19 20 24 25 26 27 28 29 30 31 32 33
chain bonds :
2-7 7-8 8-9 9-10 9-11 11-12 11-13 12-14 12-21 14-15 21-22 22-23 22-34
24-36 34-35 34-36 35-37 35-38 38-39 38-40 40-41 41-42 42-43 43-44 43-45
43-46 46-47 46-48
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20 24-29
24-25 25-26 26-27 27-28 27-30 28-29 28-33 30-31 31-32 32-33
exact/norm bonds :
8-9 9-10 9-11 11-13 12-21 21-22 22-23 34-35 35-37 35-38 38-39 43-46
exact bonds :
2-7 7-8 11-12 12-14 14-15 22-34 24-36 34-36 38-40 40-41 41-42 42-43
43-44 43-45 46-47 46-48
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20 24-29
24-25 25-26 26-27 27-28 27-30 28-29 28-33 30-31 31-32 32-33

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom
19:Atom 20:Atom 21:CLASS 22:CLASS 23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom
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37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS 43:CLASS 44:CLASS
45:CLASS 46:CLASS 47:CLASS 48:CLASS

10649386

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L6      STRUCTURE UPLOADED

=> d l6
L6 HAS NO ANSWERS
L6              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


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SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
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PROJECTED ANSWERS:               0 TO        0

L7            0 SEA SSS SAM L6

=> s l6 ful
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SEARCH TIME: 00.00.01

L8            2 SEA SSS FUL L6

=> file caplus
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                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     155.42     328.48

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00      -0.69

FILE 'CAPLUS' ENTERED AT 16:18:45 ON 19 MAY 2004
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5/13/2004



FILE COVERS 1907 - 19 May 2004 VOL 140 ISS 21
FILE LAST UPDATED: 18 May 2004 (20040518/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s l8
L9 2 L8

=> d abs bib hitstr 1-2

L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

AB Compds. that are ligands for the receptor GHS-R 1A, as well as pharmaceutically acceptable salts thereof, are useful for the manufacture of medicaments for the regulation of food intake.

AN 2001:581723 CAPLUS

DN 135:147451

TI Use of compounds for the regulation of food intake

IN Andersen, Maibritt Bansholm; Hansen, Birgit Sehested; Raun, Kirsten; Tullin, Soren; Thim, Lars

PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001056592 | A1 | 20010809 | WO 2001-DK64 | 20010129 |
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| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
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| | US 2004063636 | A1 | 20040401 | US 2003-649386 | 20030827 |
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| | DK 2000-1107 | A | 20000717 | | |
| | US 2000-181303P | P | 20000209 | | |
| | US 2001-771770 | B1 | 20010129 | | |

IT **267225-30-9**, NNC 26-1187

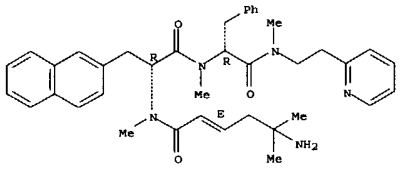
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of compds. for regulation of food intake that are ligands of growth hormone secretagogue type 1A receptors (GHS-R 1A) in relation to growth hormone release)

RN 267225-30-9 CAPLUS

CN D-Phenylalaninamide, N-[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N,Nα-dimethyl-N-[2-(2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

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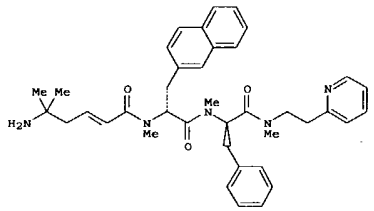

I

AB The invention relates to novel compds., compns. containing them, and their use for treating medical disorders resulting from a deficiency in growth hormone. Preparation of e.g. I is described.

AN 2000:314733 CAPLUS

DN 132:318046

TI Compounds with growth hormone-releasing properties

IN Ankersen, Michael; Richter, Lutz Stefan

PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| | US 1998-107663P | P | 19981109 | | |

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

WO 1999-DK594 W 19991103

OS MARPAT 132:318046

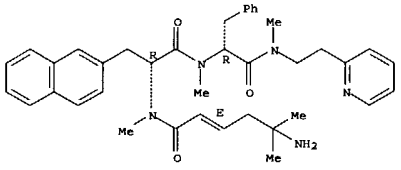
IT **267225-30-9P 267225-40-1P**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(compds. with growth hormone-releasing properties)

RN 267225-30-9 CAPLUS

CN D-Phenylalaninamide, N-[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N,Nα-dimethyl-N-[2-(2-pyridinyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 267225-40-1 CAPLUS

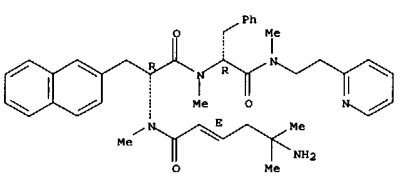
CN D-Phenylalaninamide, N-[(2E)-5-amino-5-methyl-1-oxo-2-hexenyl]-N-methyl-3-(2-naphthalenyl)-D-alanyl-N,Nα-dimethyl-N-[2-(2-pyridinyl)ethyl]-, monoacetate (9CI) (CA INDEX NAME)

CM 1

CRN 267225-30-9

CMF C39 H47 N5 O3

Absolute stereochemistry.
Double bond geometry as shown.



L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CM 2

CRN 64-19-7
CMF C2 H4 O2

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT